

-continued

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 <220> FEATURE:
 <223> OTHER INFORMATION: FGF21 secretion constructs, cloned into pVK7ara
 (Nde/Eco)

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<210> SEQ ID NO 44
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 (Nde/Eco)

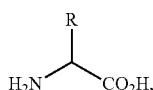
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 20

What is claimed is:

1. A composition comprising a pharmaceutically acceptable carrier and a modified FGF-21 polypeptide comprising a non-naturally encoded amino acid, wherein:

- (a) the modified FGF-21 polypeptide comprises a sequence at least 90% identical to SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, or SEQ ID NO: 7;
- (b) the non-naturally encoded amino acid has the structure:



wherein the R group is any substituent other than the side chain found in alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine, pyrrolysine, or selenocysteine;

- (c) the modified FGF-21 polypeptide contains a substitution of an amino acid with the non-naturally encoded amino acid at position 108 of SEQ ID NO: 1 or the corresponding amino acid position in SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, or SEQ ID NO: 7;
- (d) the modified FGF-21 polypeptide maintains the biological activity of human FGF-21 polypeptides;
- (e) the non-naturally encoded amino acid is linked to a linker, polymer, or biologically active molecule; and
- (f) the modified FGF-21 polypeptide has an in vivo half-life at least two-fold greater than the human FGF-21 polypeptide of SEQ ID NO: 1.

2. The composition of claim 1, wherein the non-naturally encoded amino acid is a phenylalanine derivative or is para-acetyl-L-phenylalanine.

3. The composition of claim 1, wherein (i) the non-naturally encoded amino acid comprises a first functional group and the linker, polymer, or biologically active molecule comprises a second functional group, wherein the first functional group and second functional group are not identical and each comprise a carbonyl group, an aminooxy group, a hydrazide group, a hydrazine group, a semicarbazide group, an azide group, or an alkyne group; or (ii) the first functional group on the non-naturally encoded amino acid is a carbonyl moiety and the second functional group on the linker, polymer, or biologically active molecule is an aminooxy moiety, and the resultant covalent linkage created by the reaction of the first and second functional groups is an oxime linkage.

4. The composition of claim 1, wherein the polymer comprises (i) a polysaccharide; (ii) a poly(ethylene glycol); or (iii) a poly(ethylene glycol) having an average molecular weight of between about 0.1 kDa and about 100 kDa.

5. The composition of claim 1, wherein said pharmaceutically acceptable carrier comprises one or more of saline, buffered saline, dextrose, water, glycerol, ethanol, buffers, antioxidants, low molecular weight polypeptides, proteins, hydrophilic polymers, amino acids, monosaccharides, carbohydrates, chelating agents, divalent metal, sugar alcohols, salt-forming counter ions, nonionic surfactants, surfactants, ethylene/polypropylene block polymers, bulking agents, tonicity modifiers, and/or preservatives.

6. The composition of claim 1, which is sterile, and/or is a powder, granule, or tablet.

7. A unit dose container comprising the composition of claim 1.

8. The unit dose container of claim 7, wherein the composition is provided in an injectable form.

9. A composition comprising a pharmaceutically acceptable carrier and a modified FGF-21 polypeptide comprising a non-naturally encoded amino acid, wherein:

- (a) the modified FGF-21 polypeptide comprises a sequence at least 95% identical to SEQ ID NO: 1, SEQ